Remarks

The Office Action mailed January 27, 2004, has been received and reviewed. Claims 32, 45, and 67 having been amended, the pending claims are claims 30-33 and 35-70. Reconsideration and withdrawal of the rejections are respectfully requested.

Claim 32 is amended to change "is" to "are," claim 45 is amended to delete "comprising" and insert "comprises" therefor, and claim 67 is amended to insert "the" before "subunit" and "fragment." It is applicants' position that these amendments do not limit the scope of the claims.

Status of claims

At paragraph 16 of the Action, page 6 of the Action, the Office states that claims 32, 37-43, 45, 67, 68, and 70 stand rejected; however, the Action does not include a rejection of claim 68 or claim 70. The Office is requested to note that claims 68 and 70 are allowable. If the Office intended to include claims 68 and/or 70 in a rejection in the present Action, then applicants' request that the next Office Action, if any, be made non-final to give the applicants a full and fair opportunity to address the rejection.

The 35 U.S.C. §112, Second Paragraph, Rejection

The Office rejected claims 32, 45, and 67 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claim 32 was rejected as "incorrect and/or confusing in the recitation nucleotides . . . . . is operably linked.' It is unclear whether nucleotides 73 to 309 are operably linked, or whether the nucleic acid molecule is operably linked to a promoter." It is applicants' position that the claim

is clear that nucleotides 73 to 309 are operably linked. In order to further prosecution, claim 32 has been amended to recite "nucleotides . . . are operably linked."

Claim 45 has been amended to delete "comprising" and insert "comprises" therefor.

Claim 67 has been amended to insert the word "the" before "subunit" and before "fragment."

The Office is respectfully requested to reconsider and withdraw the rejections of claims 32, 45, and 67 under 35 U.S.C. §112, second paragraph.

The 35 U.S.C. §102 Rejection

The Office rejected claims 37-40, 43 and 67 under 35 U.S.C. §102(b) as being anticipated by Sanger et al., (J. Mol. Biol., 162:729-773 (1982)). This rejection is respectfully traversed.

To begin with, the applicant respectfully submits that the Action requires clarification. The Action asserts that Sanger et al. teaches "a nucleic acid molecule comprising several long stretches of nucleotides showing 100% sequence identity with nucleotides 73 to 309 of SEQ ID NO:22 . . . . See the attached sequence search report" (Action, page 4). However, there is no attached sequence search report comparing nucleotides sequences that addresses this point and has nucleotides. The Action includes a sequence search report, but it is a comparison of two amino acid sequences. Thus, the Office has not provided proof that Sanger et al. teaches "a nucleic acid molecule comprising several long stretches of nucleotides showing 100% sequence identity with nucleotides 73 to 309 of SEQ ID NO:22."

The present rejection is based on an assertion that Sanger et al. inherently anticipates claims 37-40, 43 and 67.

A. Standard for establishing inherent anticipation

"The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." M.P.E.P §2112 (emphasis in original). "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." M.P.E.P §2112 (emphasis in original). It is respectfully submitted that the Office has not met its burden of providing a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristics necessarily flow from the teachings of Sanger et al.

B. Sanger et al. does not inherently teach an operably linked regulatory or control sequence.

According to the Action, Sanger et al. discloses a nucleotide sequence encoding a polypeptide having the sequence KTVDAAKICGGAENVVKTETQQTFVNGLLGFIT, and notes that this polypeptide is depicted at Figure 6 of Sanger et al. The Action also states that "[t]he fact that the protein or polypeptide was expressed (see page 762) indicates that the prior art nucleotide sequence inherently contained a regulatory or control sequence" (Action, page 4).

Sanger et al. does not teach or suggest that the polypeptide is expressed. Figure 6 of Sanger et al. lists the gamma strand in the region 46,452 to 47,500 (see legend to Fig. 6). Contrary to the Office's assertion, page 762 of Sanger et al. says nothing about the expression of any proteins encoded by the gamma strand in the region 46,452 to 47,500.

Sanger et al. comments on the two possible reading frames present in the sequence depicted at Figure 6 of Sanger et al. (see page 768, the fifth paragraph). Specifically, Sanger et al. states that in the sequence of Figure 6 "there are two possible reading frames . . . with acceptable SD

sequences," but also states that "[a]s far as we know, there is no other evidence for leftward transcription or for gene products in this region" (see page 768, the fifth paragraph). Furthermore, the gene map at Figure 1 of Sanger et al. shows the reading frame containing the sequence KTVDAAKICGGAENVVKTETQQTFVNGLLGFIT as a box with broken lines containing the number 97 (see right side of right arm in Fig. 1, page 734 of Sanger et al.). The legend to Figure 1 states that "[b]oxes with broken lines indicate the more speculative reading frames," and that "[w]here no gene or protein product has been assigned to an open reading frame (orf) it has been assigned a number." Thus, Sanger et al. does not teach or suggest that the polypeptide described therein is expressed.

The Office's conclusion "that the prior art nucleotide sequence inherently contained a regulatory or control sequence" (Action, page 4) is based on the assumption that the polypeptide encoded by the nucleotide sequence was expressed. There is no evidence in Sanger et al. that the polypeptide was expressed, thus, the Office's conclusion cannot be correct. Accordingly, the Office has not provided any evidence that the prior art nucleotide sequence necessarily contained a regulatory or control sequence, and therefore the Office cannot rely upon a theory of inherency under 35 U.S.C. §102(b).

Independent claim 37 recites "an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising an avian *E. coli* Iss polypeptide or an immunogenic fragment or immunogenic subunit thereof, wherein the nucleic acid molecule further comprises at least one regulatory sequence or control sequence operably linked to the nucleotide sequence encoding the polypeptide . . . ." Sanger et al. does not teach such a nucleotide sequence encoding such a polypeptide or an immunogenic fragment or immunogenic subunit thereof, wherein the nucleotide sequence further comprises at least one regulatory sequence or control sequence operably linked to the nucleotide sequence encoding the polypeptide. Since Sanger et al. does not teach every element of independent claim 37, Sanger et al. does not anticipate independent claim 37.

C. Summary

For at least these reasons, the Office is respectfully requested to reconsider and withdraw the rejection of claims 37-40, 43 and 67 under 35 U.S.C. §102(b) as being anticipated by Sanger et al., (J. Mol. Biol., 162:729-773 (1982)).

The first 35 U.S.C. §103 Rejection

The Office rejected claims 37 and 41 under 35 U.S.C. §103(a) as being unpatentable over Sanger et al., (J. Mol. Biol., 162:729-773 (1982)) in view of Applicants' admitted state of the prior art. This rejection is respectfully traversed.

The burden is on the Office to establish a *prima facie* case of obviousness of the claimed invention, and it is respectfully argued that the Office has fallen short of meeting this burden. In particular, the Office has failed to establish at least criterion i as set forth below of the three basic criteria of a *prima facie* case of obviousness.

The three criteria that must be met to establish a *prima facie* case of obviousness are:

(i) there must be a suggestion or motivation, either in the documents themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the document or to combine document teachings;
(ii) there must be a reasonable expectation of success; and
(iii) the prior art document (or documents when combined) must teach or suggest all the claim limitations. (MPEP § 2143)

It is respectfully submitted that there is no motivation to modify Sanger et al. to arrive at the present invention. The Office asserts that "[o]ne of skill in the art would have been motivated to produce the instant invention for the expected benefit of improved expression of Sanger's polynucleotide since improved expression is ideally desired in the art" (Action, page 5). According to the Manual of Patent Examining Procedure,

> "The initial burden is on the examiner to provide some suggestion of the desirability of doing what the inventor has done. To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references." MPEP §706.02(j) (emphasis added). Moreover, "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." In re Mills, 16 USPQ2d 1430 (Fed Cir. 1990); MPEP §2143.01 (emphasis added).

The statement made by the Office at page 5 of Action may show that the document could be modified to have a regulatory sequence or control sequence operably linked to the nucleic acid molecule of Sanger et al.; however, it does not provide any convincing line of reasoning as to why a skilled person would combine the documents.

As discussed above, Sanger et al. does not teach or suggest that the reading frame containing the sequence KTVDAAKICGGAENVVKTETQQTFVNGLLGFIT is expressed. Sanger et al. does not provide any motivation for operably linking the reading frame containing the sequence KTVDAAKICGGAENVVKTETQQTFVNGLLGFIT to a regulatory sequence or a control sequence. The Office has not provided any evidence or convincing reasoning why the skilled person would have any desire to take the nucleotides disclosed at Figure 6 of Sanger et al., and operably link them to a regulatory sequence or control sequence (claims 37 and 41).

Furthermore, Sanger et al. discloses a *bacteriophage*, and this bacteriophage does not infect animal cells. The skilled person would not be motivated to express the bacteriophage derived reading frame containing the sequence KTVDAAKICGGAENVVKTETQQTFVNGLLGFIT in an animal cell. The Office has not provided any evidence or convincing reasoning why the skilled person would have any desire to take the nucleotides disclosed at Fig. 6 of Sanger et al.,

and operably link them to a regulatory sequence or control sequence that causes expression of the polypeptide in an animal cell (claim 41).

For at least these reasons, the Office is respectfully requested to reconsider and withdraw the rejection of 37 and 41 under 35 U.S.C. §103 as being unpatentable over Sanger et al., (J. Mol. Biol., 162:729-773 (1982)) in view of Applicants' admitted state of the prior art.

The second 35 U.S.C. §103 Rejection

The Office rejected claim 42 under 35 U.S.C. §103(a) as being unpatentable over Sanger et al., (J. Mol. Biol., 162:729-773 (1982)) and Krieg et al. (WO 96/02555). This rejection is respectfully traversed.

It is respectfully submitted that there is no motivation to combine Sanger et al. and Krieg et al. to arrive at the present invention. The Office asserts that "[o]ne of skill in the art would have been motivated to produce the instant invention for the expected benefit of further enhancing the immune response to Sanger's product" (Action, page 6).

The statement made by the Office at page 6 of Action may show that the documents could be combined to have the Sanger et al. product together with Krieg's immunostimulatory sequence; however, it does not provide any convincing line of reasoning as to why a skilled person would combine the documents.

As discussed above, Sanger et al. does not teach or suggest that the reading frame containing the sequence KTVDAAKICGGAENVVKTETQQTFVNGLLGFIT is expressed. The bacteriophage lambda has been the subject of genetic analysis for decades, and, according to Sanger et al., "[o]ther that the cos site, no function has yet been ascribed to this region" (see page 768 of Sanger et al.). The skilled person would not be motivated to further enhance an immune

response to a polypeptide that, according to Sanger et al., is only hypothetical. The Office has not provided any evidence or convincing reasoning why the skilled person would have any desire to take the nucleotides disclosed at Figure 6 of Sanger et al., and express them together with the immunostimulatory oligonucleotide sequence of Krieg et al.

For at least these reasons, the Office is respectfully requested to reconsider and withdraw the rejection of 42 under 35 U.S.C. §103(a) as being unpatentable over Sanger et al., (J. Mol. Biol., 162:729-773 (1982)) and Krieg et al. (WO 96/02555).

Amendment and Response
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Summary

It is respectfully submitted that the pending claims 30-33 and 35-70 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
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CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 27th day of APRIL, 2004, at 1:09 PM (Central Time).

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